b.) Remarks

The claims have been amended in order to recite the present invention with the specificity required by statute. The subject matter of each change is discussed below so the Examiner will understand that no new matter has been added.

At the outset, the term "up and down" has been removed from claims 42, 44, 63 and 64. It will be understood that the orientation of the pair of punches is not a salient feature of either the present invention or the Examiner's search. Accordingly, entry of this amendment requires neither further consideration nor additional search. These claims are also amended to recite that the molding material contains no lubricant (rather than the molding material does not contain a lubricant). Since this amendment is in conformity with the tablets of prior claims 54 and 55 and Applicants' previous remarks, this amendment too requires no further consideration or search. Claims 42-45, 54, 55, 63 and 64 are also amended for better syntax or idiomatic format.

The Examiner objected to the amendment dated June 4, 2004 under 35 U.S.C. §132 because it introduces new matter into the disclosure. Claims 42-70 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement for this reason. The points raised by Examiner are each addressed, serially, below.

First, the Examiner has objected to the phrase "essentially only on a surface". While Applicants respectfully suggest those of ordinary skill readily understand what such means in this art, from the specification as filed, that term is deleted solely in order to reduce the issues herein.

As to the molding material "not containing lubricant", such subject matter is disclosed in the specification as filed, e.g., at page 11, lines 22-23. As to the coating film "remaining intact", such subject matter is disclosed in the specification as filed at page 14, lines 5-6. Additionally, as to the function of the matrix being "maintained", such subject

matter is disclosed in the specification as filed at page 14, lines 8-9. Finally, as to the granule "remaining intact", such subject matter is disclosed in the specification as filed at page 18, lines 20 et seq.

The Examiner also questioned where "enhancing" the function of a compressed tablet is disclosed. In response, such has been amended in conformity with specification page 1, lines 8-11, page 7, lines 8-9 and from page 8, line 20 to page 9, line 9.[1/]

The Examiner also objects to the specification for improperly incorporating essential material by reference to a foreign application or patent. In this regard, the Examiner refers to the citation of various Japanese laid-open applications, e.g., at page 6, lines 20-25. In response, Applicants wish to point out that no essential material is incorporated therein. Rather, such citations only evidence the state of the art at the time this application was filed.

Claims 42-70 stand rejected under 35 U.S.C. §103(a) as being obvious over Morimoto (EP 0 650 826 A1), in view of Roche (U.S. Patent No. 5,075,114). Claims 42-70 are also rejected as being obvious over Tsushima (U.S. Patent No. 6,036,974) in view of Roche.

As the Examiner is aware, the present invention relates to a method for maintaining the function of an active substance without destroying granules including (i) a coated active substance or (ii) an active substance being in a base matrix. The present invention also relates to a compressed tablet in which the function of the granule is not damaged, and to its production method.

By way of background, generally, when a molding material including coated granules or granules of active substance in a base matrix is tabletted, the structure of the

---

1/ The specification utilizes the term "keeping" whereas the more idiomatic and synonymous term --maintaining-- has been utilized in the claims. See Oxford American Dictionary (2001) at 929.

granules is destroyed by pressure and the function of the granules is damaged.

In contrast, the present invention maintains the function of an active substance by not physically destroying the granules. As such, a tablet with superior properties, e.g., without loss of sustained release function or enteric property, can be produced. As seen below, the tablet can maintain the properties of the untabletted granules in these matters.

Neither these features, nor the advantages of the same, are taught by the cited art.

Morimoto discloses a tabletting machine for applying a lubricant on the surface of a tablet to prevent sticking. However, Morimoto conventionally tablets powdered or granular pharmacological agents, not granules including active substance coated with film, or granules including active substance in a base matrix, as recited in the pending claims.

Roche teaches a pharmaceutical tablet comprised of particle coated with polymer blend. The coated particle is compressed to a tablet with a tabletting machine.

The Examiner suggests that it would have been obvious for a person skilled in the art to utilize Roche's material in Morimoto's process, taken with Tsushima, which itself discloses an aqueous tablet in which a lubricant is applied on its surface in order to prevent sticking during production.

However, as with Morimoto, Tsushima does not disclose or suggest use of granules including active substance covered with a coating film, or the granule including active substance in a base matrix.

Respectfully submitted, at the outset, it is not seen that there are any common technical problems sought to be addressed among Roche, Morimoto and Tsushima and so, no motivation for combining them. Since their technical ideas and goals differ in kind, it is not seen why they would be combined absent the suggestions of

Applicants' disclosure, and so, at least for this reason, there is simply no *prima facie* obviousness.

Moreover, in any event, even assuming arguendo that there is *prima facie* obviousness, such is overcome by the unexpected improvements achieved by the present invention. Applicants discussed these improvements previously, but they were apparently disregarded because the Examiner states there is no side-by-side comparison of the present invention to the closest embodiment of Morimoto or Tsushima. In response, Applicants explain clearly below how the results of Table 2 exactly represent such side-by-side comparison.

As shown in the specification, the tablet achieved by the present invention is superior in its rapid disintegrability and hardness comparing to the tablets described in the cited references and has such properties that the functions of micro capsule granule such as sustained release and enteric functions are not diminished. These data provide the results of comparative experiments of the present invention and the closest embodiments of the prior art, as explained to complete the record in detail below.

Tables I and II (attached at Tab A) show the composition of the tablets produced in experiment 3 and experiment 4. Such compositions are described from page 62, line 5 to page 64, line 19. The amount of lubricant applied on the surface of the tablet of the experiment 4 is 0.03 % by weight as described in the experiment 1 of the embodiment of the invention 1 (see page 46, line 17 to page 47, line 7).

Then, 1 % by weight lubricant is added to Roche's molding material (sustained release microcapsule granule containing theophylline) and Morimoto's microcapsule (formed with enteric coating) and tabletted. Compared to those tablets is the tablet of the present invention in which lubricant is not contained in the molding material and is applied only on the surface thereof. As shown in Table III, Roche's and Morimoto's tablets were substantially less hard when tabletted at the same pressure -- they achieved no

more than 40% of the hardness of the present invention.

While this unexpected improvement alone is useful to those of ordinary skill and therefore, sufficient to rebut any *prima facie* case of obviousness, there are still other showings also sufficient to do so, already of record, as discussed below.

Table IV shows the comparison result of (i) sustained release of the tablet in Applicants' experiment 5, (ii) experiment 5 (divided) in which the tablet in experiment 5 is divided into two, and (iii) the tablets produced from Morimoto's granules (in comparison 7). The granule of Morimoto per se is also utilized for comparison as "Reference 1". As clearly shown in Table IV, even if the tablet of the present invention is divided, it still shows the same sustained release characteristics as the untabletted granules of Morimoto. However, in the comparison 7 (using tablets produced from Morimoto granules), the release time is drastically reduced because Morimoto's granules are destroyed.

Finally, Table V compares sustained release of (i) the tablet in Applicants' experiment 6, (ii) experiment 6 (divided) in which the tablet in experiment 6 is divided into two, and (iii) the tablets produced from Roche's granules (comparison 8). The granule of Roche per se is also shown for comparison as "Reference 2". Again, as clearly shown in Table V, even if the tablet of the present invention is divided, it still shows the same enteric ability as the untabletted granules of Roche. However, in comparison 8 (using Roche's tabletted granules) the active ingredient is released in less than 35% of the sustained release period of the present invention because Roche's granules are destroyed.

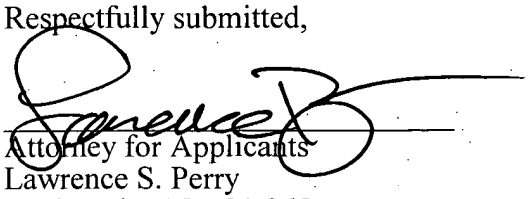
Again, these remarkable improvements are all of great utility to those of ordinary skill in the art, and none is even remotely suggested thereby. Accordingly, any *prima facie* obviousness is necessarily rebutted.

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 42-70 remain presented for continued prosecution.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,



Attorney for Applicants
Lawrence S. Perry
Registration No. 31,865

FITZPATRICK, CELLA, HARPER & SCINTO
30 Rockefeller Plaza
New York, New York 10112-3801
Facsimile: (212) 218-2200

LSP\ac

NY_MAIN 469171v1

Table 1

	experiment 3	comparison 4
granule of reference 1	1000g	1000g
lactose	700g	700g
crystalline cellulose	300g	280g
magnesium stearate (to be mixed with molding material)	0g	20g (1.0% by weight)
magnesium stearate (to be applied on tablet's surface)	0.07 % by weight	0 % by weight

Table 2

	embodiment 4	comparison 5
granule of reference 2	500g	1000g
lactose	350g	700g
crystalline cellulose	150g	280g
magnesium stearate (to be mixed with molding material)	0g	20g (1.0% by weight)
magnesium stearate (to be applied on tablet's surface)	0.03 % by weight	0 % by weight

Table 3 (rewritten from table 3 in specification)

tableting pressure (kg/punch)	tablet hardness			
	experiment 3	comparison 4	experiment 4	comaparison 5
500	5.0 (tablet of experiment 5)	2.0	5.5 (tablet of experiment 6)	2.0
1000	10.0	4.5 (tablet of comparison 7)	11.0	5.0 (tablet of comparison 8)
1500	14.0	9.0	15.0	9.5

table IV (data is rewritten from tables 4 and 5 in specification)

elution time (hr)	solution	experiment 5	experiment 5 (divided)	comparison 7	reference 1
0	Japanese Pharmacopoeia first solution	0	0	0	0
0.25		5	7	15	5
0.50		12	13	40	10
0.75		15	16	65	15
1.00		22	23	80	20
1.50		30	41	95	30
2.00		41	52	100	40
(2.00)	Japanese Pharmacopoeia second solution	41	52	100	40
2.50		51	64	100	50
3.00		61	83	100	60
4.00		82	100	100	80
5.00		100	100	100	100

table V (data is rewritten from tables 4 and 5 in specification)

elution time (hr)	solution	experiment 6	experiment 6 (divided)	comparison 8	reference 2
0	Japanese Pharmacopoeia first solution	0	0	0	0
0.25		0	0	30	0
0.50		0	0	70	0
0.75		0	0	95	0
1.00		0	0	100	0
1.50		0	1	100	0
2.00		2	3	100	1
(2.00)	Japanese Pharmacopoeia second solution	2	3	100	1
2.50		55	60	100	60
3.00		100	100	100	100
4.00		100	100	100	100
5.00		100	100	100	100